UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,349	08/19/2003	Robert Seid	2300-1357.10 (PP01357.124	3803

27476 7590 09/30/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,349	SEID, ROBERT	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,32 and 43-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31, 32 and 43-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *81903*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendment

1) Acknowledgment is made of Applicant's preliminary amendment filed 08/19/03. With this, Applicant has amended the specification.

Status of Claims

2) Claims 1-30 and 33-42 have been canceled via the amendment filed 08/19/03.

Claims 31 and 32 have been amended via the amendment filed 08/19/03.

New claims 43-49 have been added via the amendment filed 08/19/03.

Claims 31, 32 and 43-49 are pending and are under examination.

Information Disclosure Statement

3) Acknowledgment is made of Applicant's information disclosure statement filed 08/19/03. The information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

4) This application is a Divisional of application of 08/908,262, filed 08/07/1997, *now U.S. patent 6,638,513,* and claims priority to the provisional application, SN 60/024,454 filed on 27 August 1996.

Title

5) The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. A new title --A method of producing *Neisseria meningitidis* serogroup B glycoconjugates-- is suggested.

Specification - Informalities

6) The instant specification is objected to for the following reason(s):

(a) The amendment made to the first paragraph of the specification via the preliminary amendment filed 8/19/03 does not accurately reflect the status of the prior application(s) as indicated above 'Priority'.

(b) The use of trademarks in the instant specification has been noted in this application. For example, 'Tween 80' on pages 24 and 25; 'Span 85' on page 25; 'Sephadex G-100' on pages 28 and 36; and 'Sephadex G-25' on page 25. The recitations should be capitalized wherever they appear and be accompanied by the generic terminology. Each letter of the

trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever such recitations appear.

(c) The 'Brief Description of the Figures' on page 6 of the specification for Figure 5 is incorrectly numbered and/or referred to. The recitation 'Figure 5' in line 21 of page 6 of the specification should be replaced with --Figures 5A and 5B--. All references to this Figure in the specification should be amended to reflect these changes in numbering.

Double Patenting

7) The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

8) Claims 31, 32 and 43-49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of the U.S. Patent 6,638,513. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined claim is not patentably distinct from the reference claim(s) because

the examined claim(s) is either anticipated by, or would have been obvious over, the reference claim(s). See e.g., *In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998)*; *In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993)*; *In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir, 1985)*. Although the conflicting claims are not identical, they are not patentably distinct from each other, because the glycoconjugate of the above-identified claims of the issued patent falls within the scope of the glycoconjugate claimed in the instant claims. Therefore, instant claims are anticipated by claims 1-7 of the U.S. Patent 6,638,513.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

9) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

10) Claims 31, 32 and 43-49 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 31, 32, 44 and 47-49 are indefinite and confusing in the recitation: 'derivatives' or 'derivative', because it is unclear what is encompassed in this recitation. What constitutes a derivative, and how much of the MenB OS's original structure has to be retained such that the resulting product can be considered a 'derivative' is not clear. The metes and bounds of the structure encompassed in the limitation 'derivative' or 'derivatives' is indeterminate.

(b) Claims 31, 32 and 47 are vague and indefinite, because it is unclear what the abbreviation 'Dp' stands for. It is suggested that Applicant use the full terminology at first occurrence in the independent claim(s) with the abbreviation retained within parentheses.

(c) Claims 31 and 32 are vague and indefinite in the recitation 'a reducing end of the derivatives' as opposed to --the reducing end of the derivatives--. Does it mean that the derivatives comprise more than one reducing end?

(d) Claims 31 and 32 are vague and indefinite in the limitation: 'the end-activated MenB OS derivatives' (see part d of the claims). For proper antecedence, it is suggested that Applicant replace the recitation with --the single end-activated MenB OS derivatives--.

(e) Claims 31 and 32 are vague and indefinite in the limitation: 'substantially homogeneous' (see parts b and d of the claims), because it is unclear what is encompassed in this phrase. The specification does not provide a standard for ascertaining the requisite degree of homogeneity that qualifies as substantial homogeneity. The metes and bounds of the claims are indeterminate.

(f) Claims 31 and 32 are indefinite in the limitations: 'MenB OS moieties' (see last line(s)) and 'MenB OS derivatives', because it is unclear how one differs from the other structurally, conformationally, or scope-wise. What are used for the production of the claimed glycoconjugate in steps (a) through (d) are 'MenB OS derivatives'. However, what is recited as being obtained in the last step is a glycoconjugate comprising 'MenB OS moieties' as opposed to 'MenB OS derivatives'.

(g) Claims 47-49 have improper antecedence in the limitation: 'the MenB OS derivative'. Claims 47-49 depend from claim 31 or 32, which recite 'MenB OS 'derivatives' as opposed to a 'MenB OS derivative'.

(h) Claim 31 is vague in the recitation 'a carrier molecule', because it is unclear what is encompassed in this limitation. Is this a non-immunogenic carrier, immunogenic carrier, organic or inorganic carrier, pharmaceutical or non-pharmaceutical carrier, protein or non-protein carrier? Does a dipeptide linker or a single amino acid residue qualify as a 'carrier molecule'?. Is this carrier a peptide, polysaccharide, protein, nucleic acid, or a latex bead?

(i) Claims 43-49, which depend directly or indirectly from claim 31 or claim 32, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

11) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

12) Claims 31, 32 and 43-47 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Jennings *et al.* (US 5,811,102, Applicant's IDS) ('102).

Jennings *et al.* ('102) taught a glycoconjugate comprising *Neisseria meningitidis* serogroup B capsular polysaccharide fragment derivatives (i.e., oligosaccharide derivatives) in which sialic acid N-acetyl groups are replaced with N-propionyl groups, wherein such oligosaccharide derivatives are covalently attached to a carrier molecule, such as, tetanus toxoid (see Example 8). A method of producing the glycoconjugate is taught. The protein carrier in the glycoconjugate is CRM_{197} (see the sentence bridging columns 5 and 6). The conjugate was synthesized essentially as previously described and under the exact same conditions, i.e., as described in the preceding parts of the patent (see Example 8). The synthetic process and conditions are described elsewhere in the patent. The average molecular weight of the MenB oligosaccharide derivative was about 10 to 200 sialic acid residues (see column 5, lines 32-35), which encompasses the MenB OS derivatives having an average Dp of about 12 to18, or about 10 to 20 recited in the instant claims. Such materials were obtained using art known gel filtration or sizing membranes (see column 5, third paragraph). The N-propionylated MenB-tetanus toxoid conjugate disclosed in Example 8 contains modified polysaccharide fragments 'of the same molecular weight' (i.e., substantially homogenous MenB oligosaccharide derivatives). The oligosaccharide was conjugated to the carrier protein through a single binding site at the terminal end of the backbone of the oligosaccharide (see column 6, first and third full paragraphs).

Instant claims are product-by-process claims and are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicant has not shown that the alleged differences in the process result in a product that is structurally different from the product of the prior art.

Claims 31, 32 and 43-47 are anticipated by Jennings *et al.* ('102).

Rejection(s) under 35 U.S.C. § 103

13) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

14) Claims 48 and 49 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Jennings *et al.* (US 5,811,102 - Applicants' IDS) ('102) as applied to claims 31 or 32 above, and further in view of Sato *et al.* (*J. Biol. Chem.* 270 (32): 18923-18928, 1995 - Applicant's IDS) and Staveski *et al.* (US 5,354,853 - Applicant's IDS).

The reference of Jennings *et al.* ('102) in this rejection is applied, because it qualifies as prior art under subsection (e) of 35 U.S.C. § 102 and accordingly is not disqualified under U.S.C. 103(a).

The teachings of Jennings *et al.* ('102) have been explained above, which do not disclose the glycoconjugate comprising a C3-C16 long-chain aliphatic lipid covalently attached thereto.

Sato *et al.* taught a method of conjugating by reductive amination a lipid, phosphatidylethanolamine, to oligosaccharides of alpha (2->8)-linked polysialic acid (i.e. serogroup B meningococcal capsular oligosaccharide) with defined degrees of polymerization (Dp) (see abstract and page 18924). It is disclosed that lipidated oligosaccharides do show retention of the immunological epitope (see page 18927).

Staveski *et al.* disclosed a method of coupling a phospholipid such as phosphatidylethanolamine to an oligosaccharide to produce a novel phospholipid-saccharide conjugate (see abstract, column 3, lines 10-0, 45 and 46; and column 4, lines 43-50). Staveski *et al.* further taught that such conjugates can be used to produce liposomes (see column 4, lines 11 and 12).

Since the techniques of conjugating lipids to a saccharide or specifically to an oligosaccharide of alpha (2->8)-linked polysialic acid are well known in the art, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to attach Staveski's or Sato's phospholipid, phosphatidylethanolamine, to Jennings' (102) N-propionylated serogroup B meningococcal capsular oligosaccharide glycoconjugate using Staveski's or Sato's method to produce the glycoconjugate of the instant invention, with a reasonable expectation of success. Given that lipidation of oligosaccharides is routinely practiced in the art for production of liposomes as taught by Staveski *et al.*, one of skill in the art would have been motivated to produce the instant invention for the expected benefit of using Jennings' ('102) conjugate, advantageously, as a liposome preparation, for the purpose of further increasing the immunogenicity of the conjugate.

Claims 48 and 49 are *prima facie* obvious over the prior art of record.

Remarks

15) Claims 31, 32 and 43-49 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of amendments, responses or papers is (703) 872-9306.

17) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

18) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

September, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER